1898, is found a description of an interesting case of pregnancy in fibroid uterus. Abdominal section was performed and a living child delivered. Clamps were placed on the broad ligaments and the cervix was removed through the vagina. Amputation of the fibroid uterus was first performed.

A large mass of tissue was found outside the clamp on the left side. It was drawn down, another clamp placed outside, and this was removed, when it was found to be a second uterus. The patient made a good recovery.

Dangers and Treatment of Dry Labor.—Brodhead, *Medical Record*, May 14, 1898, describes well the dangers to mother and child arising from pressure in dry labor. He urges early interference, so soon as disturbances of the fœtal pulse occur. He has found, to bring on labor, the following treatment useful: A large dose of castor oil and glycerin, followed shortly by 10 grs. of sulphate of quinine repeated every three hours with $\frac{1}{30}$ gr. of sulphate of strychnine every two hours, careful watch being kept for unpleasant effects. He calls attention to the value of lysol as an antiseptic in these cases.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

W. T. COUNCILMAN, M.D.,

SHATTUCK PROFESSOR OF PATHOLOGICAL ANATOMY, HARVARD UNIVERSITY.

AND

F. B. MALLORY, M.D.,

ASSISTANT PROFESSOR OF PATHOLOGICAL ANATOMY, HARVARD UNIVERSITY.

Recent Work on the Toxin and Antitoxin of Tetanus.—F. Blumenthal (*Zeitschr. f. klin. Med.*, 1897, Bd. xxxii.), by inoculating animals with the spinal cord and organs of four cases of fatal tetanus, produced tetanic symptoms and death. As the result of his experiments he concludes that two substances capable of producing tetanic convulsions are present in the organs of individuals dying of tetanus. One of these corresponds in its action to the filtrate of bouillon cultures of the tetanus bacillus (tetano-toxin); the other, which he calls the "organ" poison, he believes to be formed by a union between the tetano-toxin and the protoplasm of the tissue cells. The tetanus antitoxin neutralizes the former, but has little effect on the latter. Thus, if the "organ" poison is present in large amount, the administration of tetanus antitoxin is of little value, because the antitoxin neutralizes only the tetano-toxin.

Metchnikoff (*Annales de l'Institut Pasteur*, November, 1897, "Recherches sur l'Influence de l'Organisme sur les Toxines") considers the laws which regulate the production of antitoxins. He arrives at the following conclusions: (1) The animal organism only is able to produce antitoxins. Lower forms of vegetable life, such as bacteria and yeasts, may destroy toxins or transform the infectious organisms into vaccines, but never cause the formation of antitoxins. (2) Invertebrates cannot produce antitoxin, as is shown by experiments on arthropodes (scorpion and larves de l'Orycites nasicornis), which when inoculated with tetanus toxin and left at a temperature of 32° C. produced no appreciable amount of antitoxin during a period of six months, though in the case of the scorpions the toxin appeared in the blood and was found to be stored in the liver in considerable quantity. (3) The production of antitoxin in vertebrates begins in the crocodile, in which animal this power is more marked than in mammals. Of cold-blooded animals the carp and the frog, if kept at a low temperature, will resist large quantities of tetanus toxin, but the toxin remains stored up in the blood for months without losing its power to produce tetanus if injected into guinea-pigs. If, however, the temperature of the animals is raised to 30° C., fatal tetanus occurs in the case of the frog, carp, or axolotl. Young alligators at 30° C. resist a dose of toxin sufficient to kill 6000 mice, and after two months their blood is decidedly antitoxic. In older animals the antitoxic power appears sooner than in younger animals—*e. g.*, the blood of an alligator weighing 4900 grammes, injected with a dose of toxin sufficient to kill 600,000 mice, after eight days showed itself to be antitoxic in a dose of 0.005 c.c. If kept at a temperature of 20° C. the alligator does not produce antitoxin. (4) In the study of warm-blooded animals he found that in the fowl antitoxic power was produced without any rise of temperature, but with marked leucocytosis. This would indicate that the production of antitoxin is not necessarily associated with febrile reaction. (5) Experiments with the blood and various organs show that, in the fowl at least, the antitoxin is stored up in the blood only, and, with the exception of the genital glands, is not localized in the organs. The antitoxic power of the genital glands is greater than that of the blood. Pericardial and peritoneal exudates of guinea-pigs are strongly antitoxic, showing that most of the antitoxin is in the fluids of the body. (6) The experiments with the lower forms of animal life (where no antitoxin is produced) make it impossible to accept the idea that immunity depends on a natural antitoxic power. (7) The evolution of the antitoxic power in the animal kingdom is more recent than the property of phagocytosis.

WASSERMAN and TAKAKI (*Berl. klin. Wochenschr.*, 1898, No. 1, "Ueber Tetanusantoxinische des normalen Centralnervensystems"), as the result of experiments, consider that the brain and cord of the guinea-pig have always an antitoxin action to the tetanus toxin which other organs of this animal do not have. They made an emulsion of the brain and cord in physiological salt solution, and added an amount of tetanus toxin several times the fatal dose. This mixture inoculated into animals produced no tetanic symptoms. Liver, spleen, kidney, bone-marrow, and blood-serum of the guinea-pig treated in the same manner did not have the same antitoxic power. The antitoxic power of the brain was always more marked than that of the cord. The fluid of the ventricles did not have this power. The central nervous system of the dove, horse, dog, and man was also found to have an antitoxic action.

A. MARIE (*Annales de l'Institut Pasteur*, "Sur les Propriétés Antitétaniques des Centres Nerveux de l'Animal Sain") reports some work along the line suggested by Wasserman and Takaki. He found the cord to be more antitoxic in its action than the brain, and that portions of the central ganglia were less active than the cortex. He does not believe that the normal nerve centres are antitoxic in the true sense of that word, but that their action is due to an intimate union between the toxin and the emulsified brain which renders the toxin inert. To prove this theory he inoculated the toxin and the cerebral emulsion separately—for example, the toxin in the fore-paw and the emulsion in the hind. In all cases the animals died of typical tetanus. If, however, the toxin and the emulsion were inoculated together the animal recovered. This he considers to indicate that the brain emulsion acts by direct contact, for if its action is antitoxic in the true sense of the word, it would become diffused, as does the antitoxic serum, and counteract the toxin even when inoculated separately.

METCHNIKOFF (*Annales de l'Institut Pasteur*, "Sur l'Influence de l'Organisme sur les Toxines," deuxième mémoire) confirms the experiments of Wasserman and Takaki, that an emulsion of the brain of a guinea-pig in salt solution mixed with tetanus toxin produced no results on inoculation. The brain of the turtle and of the fowl have but a slight action, merely retarding the appearance of symptoms and making the progress of the disease more chronic. The cord has no action. These animals are but slightly sensitive to tetanus, while the guinea-pig is exceedingly sensitive. From these facts he concludes, therefore, that animals exceedingly sensitive to tetanus have an antitoxic power in a high degree, while animals refractory to tetanus have little or none. The brain of frogs, however, which are extremely sensitive to tetanus, has absolutely no antitoxic power, even when the animal is kept at a temperature of 37° C., a fact which leads him to consider this property to be limited to mammals. In studying the comparative antitoxic power of the blood and of the central nervous system he found the blood much superior to the brain. On removing a portion of the cerebral hemisphere the antitoxic power of the blood was doubled in a few days. After seventeen days, however, the power of the blood and brain was equal. Of all the other internal organs—liver, spleen, kidney, muscles, bone-marrow, and ovaries—the latter had the greatest antitoxic power. These results do not indicate that the nervous system is the source of antitoxin production.

For the purpose of comparing the antitoxic power of the liquids of the body with that of the organs, he produced, by the inoculation of 10 c.c. of physiological salt solution into the peritoneal cavity, a peritoneal exudation. This exudation, which contained 118,000 leucocytes per c.mm., had an antitoxic power twice that of the normal blood. The pericardial exudation had an antitoxic action less than that of either the blood or the peritoneal exudation. The brain and cord had an antitoxic power one-tenth that of the blood or peritoneal exudation. The internal organs—liver, spleen, kidneys, suprarenal capsules, and bone-marrow—had an action more marked than that of the brain and cord, but less than that of the liquids. Of the organs, the kidney had the strongest action, and the spleen and bone-marrow the least. From these observations he concludes that the central nervous system is not the seat of production or the point of accumulation of the antitoxin. He does not accept the conclusion of Wasserman and Takaki, that the protective action of the normal nerve centres of the guinea-pig is due to an antitoxic action. He refers to the work of Marie, but does not agree with his theory that the toxin is destroyed by the direct action of the cerebral mixture. For if this were the case, tetanus could be as easily cured in the guinea-pig as in the mouse; but it is not. He considers the essential thing to be an increased production of leucocytes by the organism itself, as a result of the inoculation of the toxin and brain mixture. This theory he illustrates by injecting into the anterior chamber of the eye of a rabbit some tetanus toxin which produces little or no reaction. If, however, with the toxin he inoculates a portion of the cerebral tissue an intense inflammation is produced which leads to hypopyon. This reaction is much more marked than that produced by cerebral tissue alone. The immunity, therefore, is due to the leucocytosis produced by the injection of this mixture of toxin and brain; for leucocytes have the power not only to destroy bacteria, but also to destroy and alter toxic substances.

BEHRING and RANSOM (*Deutsche med. Wochenschr.*, March 24, 1898, "Ueber Tetanusgift und Tetanus Antitoxin"), as the result of experimentation, find that, when the antitoxin is added to the toxin in sufficient amount exactly to neutralize it, no symptoms are produced in animals inoculated with the mixture. In all cases in which the toxin is in excess the animal dies. An excess of toxin may be so dilute, however, that the animal recovers. It appears, therefore, that the antitoxin renders inert a definite amount of toxin, and that the toxin left over is still active.

An examination of various organs of the animals which succumb shows the toxin to be present in varying amount. The body viscera show the greatest amount, while none is found in the brain.

FERDINAND BLUMENTHAL (*Deutsche med. Wochenschr.*, March 24, 1898, "Ueber die Veränderung des Tetanusgiftes im Thierkörpers und seine Beziehung zum Antitoxin") discusses the finer changes in the nerve-cells resulting from the union with the toxin, and makes the point that these changes are not mechanical but chemical. This theory would explain those cases in which the injection of antitoxin produces no effect, for it can combine only with the toxin circulating freely in the blood and not with that which is already chemically combined with the cells.

F. RANSOM (*Deutsche med. Wochenschr.*, February 24, 1898, "Das Schicksal des Tetanusgiftes nach seiner intestinalen Einverleibung in den Meerschweinorganismus"), as the result of intestinal inoculations of tetanus toxin in guinea-pigs, finds that even in very large doses it produces no effect on an intact gastro-intestinal mucous membrane. It is not absorbed by either stomach or intestine, because neither toxin nor antitoxin appear in the blood. The toxin is finally excreted unchanged with the feces.

METCHNIKOFF (*Annales de l'Institut Pasteur*, April, 1898, "Recherches sur l'Influence de l'Organisms sur les Toxines (troisième mémoire), Toxine Tétanique et Leucocytes") reports further work in support of the theory of the destruction of toxins by leucocytes. He refers to the fact that as every bacterium contains some toxin, a cell taking up this bacterium must have some means of altering the toxin as well as destroying the bacterium. This absorption and destruction of tetanus toxin by leucocytes has been demonstrated by him in the fowl. Injection of toxin into a fowl or guinea-pig is always accompanied by a marked leucocytosis. Still further to strengthen his theory, he inoculated animals intraperitoneally with an emulsion of brain-substance mixed with tetanus toxin. Fluid withdrawn after twenty minutes showed large numbers of macrophages filled with brain-substance, while practically no brain-substance could be found lying free. As the toxin is known to adhere to the brain-substance it must be assumed that the toxin also is absorbed by the cell. In these cells the toxin probably undergoes some change by digestion, or possibly oxidation, which renders it inert.

Roux and **Borrel** (*Annales de l'Institut Pasteur*, April, 1898, "Tétanos Cérébral et Immunité contre le Tétanos"), by direct inoculation of tetanus toxin into brain-substance, produced, instead of the permanent contractures of ordinary tetanus, epileptiform crises, excitation, polyuria, and motor disturbances, forming a group of symptoms with distinct characteristics. By injection into different parts of the brain, different groups of muscles may be affected, an experiment of considerable physiological interest.

Experiments on a large number of animals showed that intracranial injections of antitoxic serum were much more efficacious for ordinary tetanus than subcutaneous injections.

That the brain-cells have not the power of storing up or producing antitoxin was shown by the fact that an immune animal did not react to a subcutaneous inoculation of toxin, but did to an intracranial inoculation. If the brain-cells contained an antitoxin they would have been able to counteract the toxin.

The resistance to tetanus in immune animals is not due to the fact that cells, particularly nerve-cells of the brain, become accustomed to or are insensible to the toxin; but to the fact that the toxin does not reach the brain. The toxin is intercepted and retained by other cells of the body which exercise a protective rôle and probably manufacture antitoxin. These cells are probably phagocytic cells. In all probability immunity against bacteria and against toxins will yet receive similar explanations.

Morax and **Elmassian** (*Annales de l'Institut Pasteur*, March 25, 1898, "Action de la Toxine Diphtherique sur les Muqueuses") find that the instillation of pure diphtheria toxin into the normal conjunctival sac of rabbits produces lesions identical with those produced by the diphtheria bacillus. The instillation was kept up for eight or ten hours, and the results appeared in from thirty-six to forty-eight hours. A dilute solution, 1 part of toxin to 4 of normal salt solution, was used. (It is hardly appropriate to speak of the conjunctiva or cornea at the end of the process of instillation as normal. No cultures from the inflamed conjunctiva are mentioned.)

V. Babes (*Berliner klinische Wochenschrift*, January 3, 1898, xxxv., No. 1, on the "Influence of Different Infections on the Nerve-cells of the Spinal Cord"). The nervous symptoms of severe infectious diseases, such as typhoid fever, diphtheria, etc., usually pass off without leaving any noticeable permanent effects. Nerve-cells, however, regenerate very slowly, and it is thought by many that complete restitution never takes place. It has been noted that many nerve-cells of adults after recovery from diseases affecting the nervous system are abnormal. The number of such altered cells could be taken as evidence of whether or not there were any symptoms of nervous disease during life.

In the old are found atrophic cells, homogeneity of the cells, a large quantity of pigment, probably arising from destruction of chromatophilic elements and lying usually in a preformed substance, which, in the form of small hyaline bodies, is arranged in masses or scattered through the cell-bodies, even extending into the axial portion of the process. In cells of certain regions (Clarke's column, parts of the anterior horn, certain nuclei of the bulb) is often found a homogeneous mass arising from changes in the cell-substance (œdema or hyaline metamorphosis), and the nucleus is pushed to the periphery. Sometimes there is pigment in the cell. Often the processes are indistinct. One may find in a group of relatively intact cells shrunken colloid or very pale elements with processes lost and nothing left of the nucleus but the nucleolus. The chromatophilic granules are pale or wholly lacking in the periphery of the cell, while they are more numerous around the nucleus. Cells with a large vacuole around the nucleus often occur. Occasionally one finds a cell which lies in a large space containing leucocytes, small epithelioid cells, pigment granules, or even chromatophilic granules or a nucleus extruded from the cell. In young children these changes are not found, with the exception of the heaping up of the chromatophilic elements about the nucleus or in a circumscribed part of the cell. The absence of any of these changes in many cases is to be explained, probably by the greater resistance of the cells, as we know that not only the cells of different individuals but also the cells of different parts of the nervous system of the same individual vary in this power of resisting injury. In animals inoculated with cholera and other infectious diseases and killed some weeks after recovery, more altered cells were found in the anterior horn than in those of non-infected animals. In typhoid fever, pyæmia, septicæmia, and scarlet fever changes were observed in the anterior horn consisting of the proliferation of cells around the vessels, of small hemorrhages, and of the presence of minute micro-organisms in the central canal and around the vessels. These changes had for site of predilection the capillary plexuses around the nerve-cells. The cells themselves showed a rarefaction of the chromatophilic substance which was becoming diffuse and vacuolated, or else a sort of coagulation of this substance, with staining of the nucleus, but not of the nucleolus. Sometimes there was a sort of œdema with vacuoles in the cell. Micro-organisms were found in considerable numbers in the central canal and anterior horns of cases in which there were no nervous symptoms.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF
EDWARD F. WILLOUGHBY, M.D.,
OF LONDON,
AND
CHARLES HARRINGTON, M.D.,
INSTRUCTOR IN MATERIA MEDICA AND HYGIENE, HARVARD MEDICAL SCHOOL.

Meat-poisoning: "Botulismus."—Much light has recently been thrown on the subject of meat-, sausage-, and fish-poisoning as a result of careful research growing out of a remarkable set of cases occurring at Ellezelles, in Belgium, reported by PROF. E. VON ERMENGHEM (*Zeitschrift f. Hygiene und Infectionskrankheiten*, xxvi. p. 1). Over twenty members of a musical society